

WHAT IS CLAIMED IS:

1. A method for determining the proliferative status of a population of endothelial cells comprising:

- 5 a) providing an array comprising a substrate having a plurality of addresses, wherein each address has disposed thereon a capture probe or oligonucleotide that can specifically bind an endothelial cell proliferative biomarker;
- b) preparing a nucleic acid test sample from a population of endothelial cells;
- c) contacting the nucleic acid sample with the array; and
- 10 d) determining an expression profile by detecting binding of the nucleic acids in the test sample to each address of the plurality of addresses present on the array, thereby determining the proliferative rate of the endothelial cells.

2. The method of claim 1 wherein the array comprises oligonucleotides that specifically binds one or more genes selected from the gene sequences set forth in Table 3 or Table 4.

15

3. The method of claim 2 wherein the array comprises oligonucleotides that specifically binds to Angpt-2, Clu (ApoJ), Cyr61 (CCN1), Endrb (Etb), Ifit-3 (Garg49), Fut-4, Plau (uPA) genes in combination with other biomarkers selected from the genes identified in Tables 3 through 6.

20

4. The method of claim 1 wherein the nucleic acid sample is prepared from a population of vascular endothelial cells obtained from a tumor biopsy.

5. The method of claim 4 wherein the sample is prepared from a cancer patient receiving treatment with a therapeutic agent intended to inhibit the proliferation of endothelial cells in tumor vasculature.

25

6. The method of claim 5 wherein the patient is being treated with a KDR kinase inhibitor.

7. The method of claim 6 wherein the patient is being treated with Compound A.

30

8. A method for screening a plurality of therapeutic agents for anti-angiogenic activity comprising: contacting a compound with a population of cells containing a polynucleotide comprising a nucleic acid sequence selected from the group consisting of the biomarkers identified in Tables 4 and Table 5 under conditions wherein said polynucleotide is being expressed, and determining a change in

35

expression of an endothelial cell proliferation signature, wherein a change in expression is indicative of anti-angiogenic activity.

9. The method of claim 8 wherein the population of cells is isolated from a tumor biopsy of a cancer patient who is being treated with a therapeutic agent intended to inhibit the proliferation of endothelial cells in tumor vasculature.

10. The method according to claim 10 wherein the therapeutic agent is a receptor-type kinase inhibitor.

11. The method of claim 8 wherein the change in of the endothelial cell expression signature is determined by hybridization to a microarray comprising oligonucleotide that can specifically bind an endothelial cell proliferative biomarker or by RT-PCR.

12. The method of claim 11 wherein the endothelial cell proliferation signature comprises capture probes or oligonucleotides that specifically binds to Angpt-2, Clu (ApoJ), Cyr61 (CCN1), Endrb (Etb), Ifit-3 (Garg49), Fut-4, Plau (uPA) genes in combination with other biomarkers selected from the genes identified in Table 5 or Table 6.

13. An array comprising a substrate having a plurality of addresses, wherein each address has disposed thereon a capture probe or oligonucleotide that can specifically bind a polynucleotide sequence of a biomarker gene selected from the group consisting of the genes comprising a proliferation signature defined in Table 3 and 4.

14. A composition comprising the biomarker genes comprising the proliferation signatures set forth in Table 3 or Table 4.

15. A composition comprising the biomarker genes comprising the expression signatures set forth in Table 5 or Table 6.

16. An endothelial cell proliferation signature comprising Angpt-2, Clu (ApoJ), Cyr61 (CCN1), Endrb (Etb), Ifit-3 (Garg49), Fut-4, and Plau (uPA) genes.